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Use of Molecular Docking Studies to Validate the Efficacy of Phytocompounds from Bee Pollen on SARS-CoV-2 and Prediction of ADMET/Toxicity Properties

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Abstract: Bee pollen, often referred to as "life-giving dust," is a nutrient-rich apitherapeutic product with potential applications in medicine and nutrition. It has been recognized for its therapeutic benefits, including the prevention of prostate issues, atherosclerosis, allergy desensitization, and cancer. The bioactive compounds in bee pollen, such as flavonoids and phenolic acids, exhibit antibacterial and antiviral properties by disrupting pathogen cell walls and inhibiting viral replication. In this study, molecular docking techniques were employed to explore the potential antiviral activity of bee pollen phytocompounds against SARS-CoV-2. Phytochemicals were docked with the SARS-CoV-2 spike protein and its receptor-binding domain (RBD) complexed with ACE2. The results revealed promising binding affinities for several compounds, with ΔG values lower than -7.0 kcal/mol, indicating strong potential for antiviral action. ADMET predictions were also conducted to assess pharmacokinetic properties and toxicity profiles, suggesting that certain compounds, such as hesperetin and catechin, showed favorable characteristics for further drug development. The study emphasizes the potential of bee pollen in the development of antiviral therapies, recommending *in vitro* and *in vivo* studies to validate these findings and further assess the safety and efficacy of these phytochemicals. This research offers valuable insights into the repurposing of natural compounds for therapeutic purposes, particularly in the context of COVID-19.

Keywords: Bee pollen, Phytocompounds, SARS-CoV-2, Molecular docking, Antiviral activity, ADMET prediction, Flavonol, Flavanone, Galangin, Pinocembrin, Caffeic acid, Phenethyl ester

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Introduction

Bee pollen is formed when nectar, pollen, or honey is aggregated with the bees' saliva through the agglutination process. In fact, organic compound is recognized as a valuable apitherapeutic product with applications in medicine and nutrition. It is touted as a superfood due to its supposedly high

nutritional and therapeutic value, which can have positive effects on human health, such as preventing prostate problems, atherosclerosis, allergy desensitization, and cancer. Bee pollen is also associated with positive effects on human health. The important physiological activities it possesses have been praised by many. Increased mitotic rates from bee pollen have been linked to increased toxin excretion, improved tissue repair, and reduced excess cholesterol. Its extreme scavenging behaviour has already been documented. It is a common custom to promote bee pollen as a healthy dietary option that is both inexpensive and potentially useful in the cosmetics industry.

Phytocompounds are biologically active compounds isolated from plants that have recently been considered for the treatment of viral diseases including coronaviruses. Conventional antiviral medicinal plants have macrophobic properties, that is why their extracts are being tested against SARS-CoV-2 (Bhattacharya *et al*., 2021). The antibacterial properties of bee pollen are caused by active substances such as flavonoids and phenolic acids, which lead to complexes with the cell wall of pathogens, disrupting the integrity of the cell wall, blocking ion channels and reducing the flow of electrons in the electron transport chain. Inhibition of bacterial RNA Pol by phenolics including flavonol, flavanone, galangin, pinocembrin, and caffeic acid phenethyl ester could be another method by which bee pollen exhibits antibacterial activity.

ACE2 receptors are more highly expressed in the lungs, heart, and kidneys, so the SARS-CoV-2 virus targets these organs to infect its host. Mpro is known to be involved in virus replication and is therefore a target for COVID-19 vaccine development (Pang *et al*., 2023). Knowledge of these molecular targets is important for drug development. Molecular docking, a bioinformatics approach that allows prediction of the binding mode of a molecule to a protein, is used for possible binding of the phytocompounds to viral proteins as a basis for studying antiviral activity (Morris and Lim-Wilby, 2008). ADMET research studies a molecule's pharmacokinetics—absorption, distribution, metabolism, excretion and toxicology. It is important to predict these properties to check the 'drug-likeness' and other related properties of compounds i.e., elements that would qualify a compound for therapeutic purposes but also for good pharmacological properties (Lipinski *et al*., 2001). This study examines the ability of the phytocompounds against SARS-CoV-2 and druggability by molecular docking analyses along with ADMET and toxicity predictions in order to check their application for further drug development.

Materials and Methods

Phytocompound selection: The phytocompounds were selected from those known to have antiviral properties and those used in various traditional systems of medicine. A list of 32 phytochemicals from bee pollen that were found to have an inhibitory effect on viral proteins was selected from the literature (Didaras *et al*., 2020; Mani *et al*., 2020; Thakur and Nanda, 2020; Alagawany *et al*., 2021).

Molecular Docking Procedure: Molecular docking was performed using AutoDock Vina software. Two forms of receptor structure, namely the SARS-CoV-2 S-protein (accession code: P0DTC2) and the SARS-CoV-2 spike receptor-binding domain (accession code: P0DTC2) bound to ACE2 (accession code: Q9BYF1) were examined. Heteroatoms were removed, followed by solvent deletion, replacement of incomplete side chains, and addition of hydrogen and charges. Lastly, Gasteiger charges were added. Energy minimization of the protein structure was performed using Discovery Studio. PubChem database was used to retrieve 3D structures in SDF format. Phytocompounds were prepared using ChemDraw and optimized with the MM2 force field. The docking grid was centered on the active site of the target proteins (Trott and Olson, 2010). PreADMET, Molinspiration cheminformatics and SwissADME web servers were utilized to predict the drug-likeliness, bioactivity,

Table 1: Key ADMET parameters of important phytochemicals

Phytochemical	Molecular Formula	Molecular Weight (g/mol)	BBB Permeability	CYP2C19 Inhibition	Solubility (mg/l)	# Rotatable Bonds	Bioavailability Score	Lipinski Violations
Afzelechin	C15H14O5	274.27	0.728728	Inhibitor	769.968	1	0.55	0
Kaempferol	C15H10O6	302.24	0.286076	Inhibitor	22.0776	1	0.55	0
Epiafzelechin	C15H14O6	290.27	0.728728	Inhibitor	769.968	1	0.55	0
Quercetin	C16H10O7	314.25	0.412595	Inhibitor	1000.42	1	0.55	0

physiochemical descriptors, and pharmacokinetic characteristics of the ligands (Daina *et al*., 2017).

Docking Scoring: Binding affinities were scored in terms of Gibbs free energy (ΔG), with lower ΔG values indicating stronger binding. Compounds with ΔG values less than -7.0 kcal/mol were considered promising (Kitchen *et al*., 2004).

ADMET Prediction: ADMET properties were predicted using SwissADME and ADMETlab software. SMILES format of the ligands was directly retrieved from PubChem and fed into ADME analysis tools. Parameters such as solubility, bioavailability, and metabolism by cytochrome P450 enzymes were analyzed (Daina *et al*., 2017). Lastly, toxicity analysis was performed based on results predicted by the Lazar Toxicity Prediction tool (Maunz *et al*., 2013).

Results and Discussion

The analysis was performed on the complete spike glycoprotein of SARS-CoV-2 as well as on RBD of S-protein complexed with ACE2. There are 2 PDB files considered for each of the selected macromolecules, namely PDB ID: 6LZG, PDB ID: 6M0J, and PDB ID: 6VSB, PDB ID: 6VXX (Fig. 1). Multiple structures of the same protein were considered as there are minute differences between them i.e., the A chain length of ACE2 is 596 and 603 whereas the E chain length of S-protein S1 is 209 and 229 for 6LZG and 6M0J, respectively. Similarly, the S-protein sequence length is 1281 and 1288 for 6VXX and 6VSB, respectively.

In the case of the chosen phytochemicals, only rutin and lupeol had lipophilicity out of the range. Pgp and Cyp proteins are two main candidates responsible for the metabolism and clearance of xenobiotics from the system, their inhibition or inactivation could possibly lead to severe side effects as well as drug toxicity as it directly correlates to their bioavailability. Among all the ligands from our library, none inhibited all the Cyp-isoforms (CYP1A2, CYP2C19, CYP2C9, CYP2D6, CYP3A4) i.e., at least two of the proteins were not inhibited. The results for the bioavailability of the ligands have been depicted in the boiled egg (Fig. 1).

The toxicity predictions obtained from PreADMET were further examined and compared to predictions obtained from LazarTox, an *in silico* prediction tool. According to PreADMET all the ligands are predicted as mutagen against the AMES test except for naheedin, aradiradione, sugiol, and rutin. In addition, umbelliferone was not a suitable candidate as a therapeutic molecule since it was predicted to be a mutagen (AMES test), a carcinogen (mouse and rat model), and mutagen against all four strains of *Salmonella* species. Whilst according to LazarTox predictions, it was discovered that the toxicity profile of p-coumaric acid, ferulic acid, and quercetin was not ideal. Furthermore, for nine of the ligands namely naheedin, aradiradione, nimbin, sugiol, chlorogenic acid, ellagic acid, myricetin, rutin, and gallocatechin at least 50 % of the predictions could not be provided due to insufficient dataset. Besides these, only six ligands namely hesperetin, epicatechin, catechin, mesquitol, epiafzelechin, and afzelechin were safe based on at least five parameters. However, toxicity results cannot be taken further without confirming via *in vitro* or *in vivo* analysis.

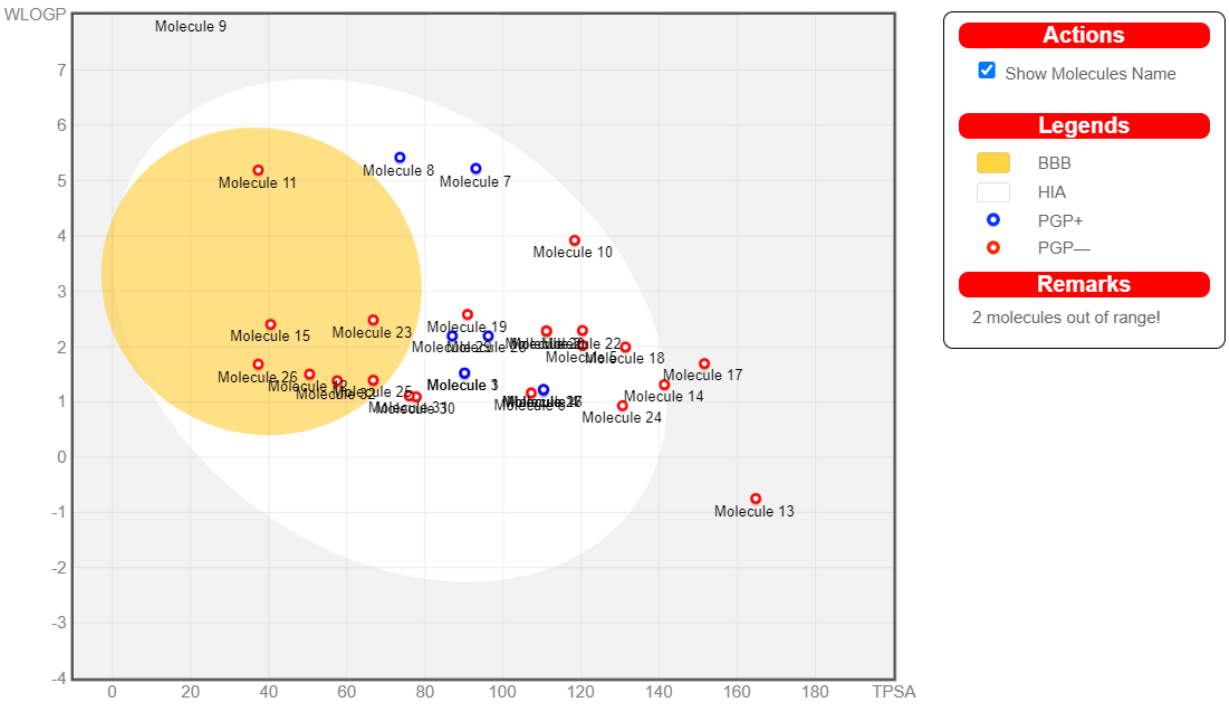

Fig. 1: Results from Wissam in boiled egg format.

In recent years, bee products are being extensively studied for their properties against SARS-CoV-2. Since, the Covid pandemic crippled worldwide (Rath *et al*., 2020), it becomes essential for researchers to develop potential antiviral drugs. Currently, we do not possess such impactful antiviral medicines. This study aims to aid in screening plausible phytochemicals with potential antiviral activity. Based on obtained predictions we can take *Apis dorsata* bee pollen for further antiviral studies. As the selected phytochemicals showed high affinity towards not only the spike protein of the SARS-CoV-2 but also the S-protein and ACE2 complex. Moreover, the easy accessibility of the product makes it an ideal candidate for further *in vitro* and *in vivo* studies to validate apitherapy. In order to further validate the obtained results, microscopy-based assays and viral internalization assays can be performed to ascertain the interaction of SARS-CoV-2 on the cell surface as well as its internalization upon treatment with bee pollen extracts. Furthermore, to validate the toxicity results *in vitro* assays need to be performed for a better understanding of how these phytochemicals present in *Apis dorsata* bee pollen could potentially be toxic or non-toxic.

Bee pollen is a promising natural supplement with potential pharmacological and physiological properties that largely depends on its botanical origin. Clinical application of standardized bee pollen as a therapeutic agent can be advocated once further research has been carried out. By classifying the bee pollen based on their botanical and geographical origin, one can gain a better understanding of their composition and properties. Additional research has to be conducted to understand the molecular mechanisms that are influenced by bee pollen besides looking for ways to nullify the side effects caused by the consumption of bee pollen.

Conclusion

The proposed outcomes of the project will be long-term sustainable since it will aid in the computational repurposing of compounds in future, reducing the development time for

medication. However, *in vitro* research is required to investigate the probable variables that serve as enhancers in viral replication, and an *in vivo* examination is required to assess the efficacy and potency of the medication employed at various phases of therapy. This study can aid researchers, scientists, and clinicians for target-based treatment since patients are given a precise mix of anti-inflammatory, antiviral, antimalarial, and immunosuppressive medicines.

Ethical Statement

The authors confirm that all ethical issues have been dealt with the research ethics guidelines provided by the Mount Carmel College (Autonomous), Bengaluru 560052, Karnataka, India

Author Contributions

Each author has equally collaborated in designing the research, conducting thorough analysis, drafting the manuscript, and refining its content. All authors have read and agreed to the published version of the manuscript.

Conflict of Interest

The authors declare no conflicts of interest.

References

Alagawany M, Farag MR, Dhama K, Malmuthuge N and Gopi M. (2021) Phytochemicals: An alternative to antibiotics and growth promoters in poultry. Front Vet Sci. 7: 617003.

Bhattacharya R, Dev K and Sourirajan A. (2021) Antiviral activity of bioactive phytocompounds against coronavirus: An update. J Virol Methods 290: 114070.

Daina A, Michielin O and Zoete V. (2017) SwissADME: A free web tool to evaluate pharmacokinetics, drug-likeness, and medicinal chemistry friendliness of small molecules. Sci Rep. 7(1): 42717.

Didaras NA, Karatasou K, Dimitriou TG, Amoutzias GD and Mossialos D. (2020) antimicrobial activity of bee-collected pollen and beebread: State of the art and future perspectives. Antibiotics 9(11): 811.

Kitchen DB, Decornez D, Felder CE and Hubbard JA. (2004) Docking and scoring in virtual screening for drug discovery: methods and applications. Nat Rev Drug Discov. 3(11): 935-949.

Lipinski CA, Lombardo F, Dominy BW and Feeney PJ. (2001) Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. Adv Drug Deliv Rev. 46(1-3): 3-26.

Mani JS, Johnson JB, Steel JC, Broszczak DA, Neilsen PM, Walsh KB and Naiker M. (2020) Natural product-derived phytochemicals as potential agents against coronaviruses: A review. Virus Res. 284: 197989.

Maunz A, Gütlein M, Rautenberg M, Vorgrimmler D, Gebele D and Helma C. (2013) lazar: a modular predictive toxicology framework. Front Pharmacol. 4: 38.

Morris GM and Lim-Wilby M. (2008) Molecular docking. Methods Mol Biol. 443: 365-382.

Pang X, Xu W, Liu Y, Li H and Chen L. (2023) The research progress of SARS-CoV-2 main protease inhibitors from 2020 to 2022. Eur J Med Chem. 257: 115491.

Rath RS, Dixit AM, Koparkar AR, Kharya P and Joshi HS. (2020) COVID-19 pandemic in India: A Comparison of pandemic pattern in Selected States. Nepal J Epidemiol. 10(2): 856-864.

Thakur M and Nanda V. (2020) Composition and functionality of bee pollen: A review. Trends Food Sci Technol. 98: 82-106.

Trott O and Olson AJ. (2010) AutoDock Vina: Improving the speed and accuracy of docking with a new scoring function, efficient optimization, and multithreading. J Comput Chem. 31(2): 455-461.